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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,063	06/22/2001	Corey E. Nislow	CYTOP003	6972

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FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER	
MILLER, MARINA I	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,063	NISLOW ET AL.	
	Examiner	Art Unit	
	Marina Miller	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5, 9-12, 14-15, 23-27, 29-30, 32-33, 37-41, 43-44, 47-53, and 55-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/7/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' submission filed on 3/07/2005 is acknowledged. Claims 2-5, 9-12, 14-15, 23-27, 29-30, 32-33, 37-41, 43-44, 47-53, and 55-56 are pending. Claims 1, 6-8, 13, 16-22, 28, 31, 34-36, 42, 45-46 and 54 are cancelled. Claims 2-5, 9-12, 14-15, 23-27, 29-30, 32-33, 37-41, 43-44, 47-53, and 55-56 presently are under examination.

Applicants' arguments have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are applied.

Information Disclosure Statement

Information Disclosure Statement (IDS) filed 3/7/2005 has been considered in part. Examiner appreciates applicant's apprising her of copending sister application listed on the IDS. References crossed out on the IDS filed 3/7/2005 have not been considered because an original application or a copy of an office action from a copending application which has not yet matured into an issued patent or otherwise become publicly available is not a proper document to be listed on PTO 1449 under 37 CFR 1.98(a).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4 and 5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 4, 5, 19, 20, 34, 35, 45, and 46 were rejected for lack of enablement in the previous Office Action mailed 12/9/2004. Applicants cancelled claims 19, 20, 34, 35, 45, and 46. Claims 4 and 5 are directed to requiring the usage of modified cell strains, which contain a deletion mutant for each non-essential gene in a parental strain. Claims 4 and 5 were rejected as being non-enabled because they recite deleting every one of the non-essential genes in a parental strain, which is unpredictable as being directed to a complex and undefined result for complex organism, as set forth in the previous office action mailed 12/9/2004. Applicants presented no arguments or amendments overcoming the enablement rejection in the reply filed 3/7/2005. Examiner maintains and reiterates the rejection from the previous office action mailed 12/9/2004.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

> having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-4, 9-12, 14-15, 23-27, 29-30, 32-41, 43-44, 47-53, and 55-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ashby, U.S. Patent 6,518,035, in view of Giuliano, U.S. Patent 6,416 and Price, U.S. Patent 5,548,661.

Claim 55 is directed to a method comprising steps of making a modified cell which features are highlighted in images of phenotypes, imaging the cells, analyzing the images with an algorithm to provide quantitative representation, and comparing the quantitative representation, wherein strains are *S. cerevisiae*, cells have been treated with drugs, and marking features comprise staining with the stain for the cell wall, genetic material and the cytoskeleton. Claims 2 and 3 limit claim 55 to particular deletion mutations. Claim 4 limits claim 55 to a deletion mutant for each non-essential gene. Claim 10 limits claim 55 to receiving the intensity versus position data and quantifying geometrical and biological information. Claim 11 limits claim 55 to quantifying both geometrical and biological information. Claim 12 limits claim 55 to comparing phenotypes with each other and clustering phenotypes to identify common traits. Claim 14 limits claim 55 to generating a database. Claim 15 limits claim 55 to linking database of claim 14 to a database of non-morphological data. Claim 56 limits claim 55 to staining with concanavalin A, DAPI, and rhodamine phalloidin.

Claim 9 is directed to a method of analyzing a collection of genetically modified strains similar to claim 55 wherein cells are stained with concanavalin A, DAPI, and rhodamine phalloidin. Claims 32-33 and 37-41 recited the same limitation as claims 2-3 and 10-15, respectively.

Claims 23-27, 29-30, 43-44, and 47-53 are directed to a computer readable medium for performing the instant methods.

Ashby discloses a method for screening (analyzing) a population of genetically modified cells of the same species that differ substantially only in the expression or activity of genes (see an abstract). Steps of the method are generally disclosed in col. 2, line 59 – col. 3, line 9 and col. 3, line 57 – col. 4, line 12. The method comprises a step of marking cell features of a genetically modified cells so that the feature is highlighted in images of the phenotypes, *e.g.*, modified and unmodified cells have different levels of target protein activity (different phenotypes, col. 8, line 23-67 and col. 11, line 8-29) wherein a modified cell also expresses a reporter gene comprising a measurable label (*e.g.*, bioluminescent, chemiluminescent, or fluorescent molecule) (col. 2, line 59 – col. 3, line 56). Ashby's method further comprises steps of imaging of modified cells to produce images of phenotypes (see fig. 1-3), analyzing the images with algorithms to provide quantitative representation of the phenotypes, and comparing the quantitative representations (col. 4, line 5-12 and col. 6, line 6-45, Brief Description of the Drawings). Ashby discloses making yeast strains encoding a reporter gene expressing a protein comprising bioluminescent, chemiluminescent, or fluorescent molecules (for example, section 5.7 and col. 3, line 45-55). Ashby discloses an application of his method for identifying drug candidates wherein cells are treated with a drug (see section 5.12, Pharmaceutical Applications; section 6.3, col. 37, line 25-67, and fig. 2-3). Ashby discloses *S. cerevisiae* strains and mutants of essential and non-essential yeast genes used in Ashby's method (sections 5.1-5.2.2, for example, col. 10, line 24-67). Ashby discloses receiving intensity versus position data from modified cells, quantifying geometric information about markers and biological information about modified cells (see fig. 2-3 and col.

6, line 6-45, Brief Description of the Drawings; see also section 6 for particular examples). Ashby discloses multiple application of his method in col. 31, line 25 through col. 35, line 60 comprising multiplex screening identical to identifying common functional traits shared by multiple genetic modifications (see section 5.9.1). Ashby teaches identifying candidate lead compounds (*i.e.*, generating a compound database) by using his method (section 5.12, col. 34, line 50-58). Ashby identified five compounds in the compound library severely inhibiting cell growth (*i.e.*, created a compound database) (section 6.4, col. 38, line 43-58). Ashby also discloses a non-morphological analysis via PCR product characterization (a secondary screening creates a PCR database) to link drug discovery data with the identity of a target gene (col. 31, line 44 – col. 32, line 3).

Although Ashby discloses making yeast cell strains that encodes a reporter gene expressing a protein comprising bioluminescent, chemiluminescent, or fluorescent molecules, he does not expressly disclose marking that comprises stain for the cell wall, genetic material and the cytoskeleton. Ashby does not disclose a computer readable medium for performing his method.

Giuliano discloses a method and system for determining activity of fluorescently labeled reporter molecules in cells in order to screen large number of compounds that specifically affect particular biological functions (*see* an abstract). Giuliano teaches using yeast cell in his method. (col. 76, line 45-51). Giuliano discloses specific cellular markers such as cell wall, genetic material, and cytoskeleton markers for imaging (col. 30, line 15-62). Cellular markers are used to measure the temporal and spatial distribution, content, and activity of intracellular components (col. 14, line 47-52). Giuliano teaches a multiparameter approach that combines several labeling

reagents in a single cell as a powerful new tool for drug discovery (col. 14, line 56-58, col. 37, line 23-47). Giuliano teaches simultaneous labeling different cellular components (col. 46, line 12-32 and col. 53, line 33 through col. 58, line 17) by using different markers such as DAPI (col. 56, line 31), rhodamine (col. 53, line 49, col. 54, line 13), and Con A (col. 54, line 15).

Either Giuliano or Price teaches a computer-based method, a program, and a computer readable medium for executing methods similar to the instant method. Giuliano discloses a computer device in col. 6, line 35 through col. 7, line 9. Price teaches fluorescent imaging utilized by Ashby and discloses his computer imaging system in col. 9, line 1 through col. 12, line 27.

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Ashby to use multiple fluorescent labeled reagent to detect genetic modifications of cells, such as taught by Giuliano, where the motivation would have been to improve the quantifying genetic modifications in drug discovery experiments within living cells, as taught by Guiliano, (col. 14, line 47-58). It would further have been obvious to one skilled in the art at the time of the invention to use a computer system, such as taught by either Giuliano or Price, to practice the method of Ashby, where the motivation would have been to improve drug discovery process, as taught by Giuliano (col. 1, line 43-45), and improve the automatization of drug discovery in order to analyze significantly greater number of cells, as taught by Price (col. 6, line 18-29).

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ashby, U.S. Patent 6,518,035, in view of Giuliano, U.S. Patent 6,416 and Price, U.S. Patent 5,548,661,as applied to

claims 2-4, 9-12, 14-15, 23-27, 29-30, 32-41, 43-44, 47-53, and 55-56 above, and further in view of Winzeler, Science, 285:901-906 (6 August 1999).

Claim 5 limits claim 55 the collection of genetically modified strains provided by *S. cerevisiae* Deletion Consortium.

Ashby, Giuliano, and Price make claim 55 obvious, as set forth above.

Although Ashby, Giuliano, and Price use deletion mutations of *S. cerevisiae* to practice their method, they do not discloses *S. cerevisiae* Deletion Consortium.

Winzeler discloses deletions of *S. cerevisiae* that form a database of *S. cerevisiae* Deletion Consortium.

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Ashby, Giuliano, and Price to use mutants from *S. cerevisiae* Deletion Consortium database, such as taught by Winzeler, where the motivation would have been to have an access to large amount of mutants for studying gene functions, as taught by Winzeler (p. 901).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marina Miller whose telephone number is (571)272-6101. The examiner can normally be reached on 8-5, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph. D. can be reached on (571)272-0718. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marina Miller
Examiner
Art Unit 1631

MM

MARJORIE A. MORAN
PRIMARY EXAMINER
5/26/05

Continuation of Disposition of Claims: Claims pending in the application are 2-5, 9-12, 14-15, 23-27, 29-30, 32-33, 37-41, 43-44, 47-53, and 55-56 .